

Substitute for form 1449A

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

**Complete if Known**

|                        |                                      |
|------------------------|--------------------------------------|
| Application Number     | 10/549,545                           |
| Filing Date            | May 26, 2006                         |
| First Named Inventor   | Matteucci, Mark                      |
| Art Unit               | 1626                                 |
| Examiner Name          | <del>Unassigned</del> Reitsang Shiao |
| Attorney Docket Number | 021305-003900US                      |

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|-------|---|----|---|
| Sheet | 1 | of | 4 |
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## U.S. PATENT DOCUMENTS

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|-----------------------|--------------------------------|--------------------|
| Examiner<br>Signature | /Rei Tsang Shiao/ (07/21/2008) | Date<br>Considered |
|-----------------------|--------------------------------|--------------------|

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<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WFO Standard ST 11, procedure. Applicant is to place a check



PTO/SB/08A (07-06)

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Sheet 2 of 4

## Complete if Known

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## FOREIGN PATENT DOCUMENTS

| Examiner<br>Initials* | Cite<br>No. <sup>1</sup> | Foreign Patent Document   |                     |                                   | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines,<br>Where Relevant Passages<br>or Relevant Figures Appear | T <sup>2</sup>           |
|-----------------------|--------------------------|---------------------------|---------------------|-----------------------------------|--------------------------------|--|---|--------------------------|
|                       |                          | Country Code <sup>3</sup> | Number <sup>4</sup> | Kind Code <sup>5</sup> (if known) |                                |  |   |                          |
|                       | BB                       | DE                        | 2229223             |                                   | 02-15-1973                     |  |   | <input type="checkbox"/> |
|                       | BC                       | EP                        | 648 503             | A1                                | 04-19-1995                     |  |   | <input type="checkbox"/> |
|                       | BD                       | WO                        | 04/85421            | A2                                | 10-07-2004                     |  |   | <input type="checkbox"/> |
|                       | BE                       | WO                        | 04/85361            | A1                                | 10-07-2004                     |  |   | <input type="checkbox"/> |
|                       | BF                       | WO                        | 02/96910            | A1                                | 12-05-2002                     |  |   | <input type="checkbox"/> |
|                       | BG                       | WO                        | 00/64864            | A1                                | 11-02-2000                     |  |   | <input type="checkbox"/> |

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| Examiner<br>Signature | /Rei Tsang Shiao/ (07/21/2008) | Date<br>Considered |  |
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<sup>5</sup> Kind of document by which published. <sup>6</sup> If the document is in a language other than English, the English language translation must be attached. <sup>7</sup> If the document is in a language other than English, the English language translation must be attached. <sup>8</sup> If the document is in a language other than English, the English language translation must be attached. <sup>9</sup> If the document is in a language other than English, the English language translation must be attached. <sup>10</sup> If the document is in a language other than English, the English language translation must be attached.

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /RS/



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| Substitute for form PTO/SB/08B (07-06)  |   |    |   | <b>Complete if Known</b><br><b>Application Number</b> 10/549,545<br><b>Filing Date</b> May 26, 2006<br><b>First Named Inventor</b> Matteucci, Mark<br><b>Art Unit</b> 1626<br><b>Examiner Name</b> <del>Unassigned</del> Reitsang Shiao<br><b>Attorney Docket Number</b> 021305-003900US |  |
| <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br>(Use as many sheets as necessary) |   |    |   |  |  |
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| NON PATENT LITERATURE DOCUMENTS |                                |  |                          |                 |
|---------------------------------|--------------------------------|--|--------------------------|-----------------|
| Examiner Initials *             | Cite No. <sup>1</sup>          | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.      | T <sup>2</sup>           |                 |
|                                 | BH                             | BERRY et al., "5-Nitro-furan-2-ylmethyl group as a potential bioreductively activated pro-drug system," <i>J. Chem. Soc. Perkin Trans.</i> 1:1147-1156 (1997).   | <input type="checkbox"/> |                 |
|                                 | BI                             | BORCH et al., "Synthesis and Evaluation of Nitroheterocyclic Phosphoramidates as Hypoxia-Selective Alkylating Agents," <i>J. Med. Chem.</i> 43:2258-2265 (2000).   | <input type="checkbox"/> |                 |
|                                 | BJ                             | BORCH et al., "Antitumor Activity and Toxicity of Novel Nitroheterocyclic Phosphoramidates," <i>J. Med. Chem.</i> 44:74-77 (2001).   | <input type="checkbox"/> |                 |
|                                 | BK                             | DE GROOT et al., "Anticancer Prodrugs for Application in Monotherapy: Targeting Hypoxia, Tumor-Associated Enzymes, and Receptors," <i>Current Medical Chemistry</i> , 8:1093-1122 (2001).  | <input type="checkbox"/> |                 |
|                                 | BL                             | DE JAEGER et al., "Relationship of hypoxia to metastatic ability in rodent tumours," <i>Br. J. Cancer</i> , 84(9):1280-1285 (2001).  | <input type="checkbox"/> |                 |
|                                 | BM                             | ENGLE et al., "31P NMR Kinetic Studies of the Intra- and Intermolecular Alkylation Chemistry of Phosphoramidate Mustard and Cognate N-Phosphorylated Derivatives of N,N'-Bis(2-chlorethyl)amine," <i>J. Med. Chem.</i> 25:1347-1357 (1982).                          | <input type="checkbox"/> |                 |
|                                 | BN                             | EVERETT et al., "Modifying rates of reductive elimination of leaving groups from indolequinone prodrugs: a key factor in controlling hypoxia-selective drug release," <i>Biochemical Pharmacology</i> , 63:1629-1639 (2002).   | <input type="checkbox"/> |                 |
|                                 | BO                             | EVERETT et al., "Bioreductively-Activated Prodrugs for Targeting Hypoxic Tissues: Elimination of Aspirin from 2-Nitroimidazole Derivatives," <i>Bioorganic Med. &amp; Chem. Ltrs.</i> 9:1267-1272 (1999).  | <input type="checkbox"/> |                 |
|                                 | BP                             | HAY et al., "A 2-Nitroimidazole Carbamate Prodrug of 5-Amino-1-(Chloromethyl)-3-[(5,6,7-Trimethoxyindol-2-yl)Carbonyl]-1,2-Dihydro-3H-Benz[E]Indole (Amino-Seco-CBI-TMI) for Use With Adept and Odepi," <i>Bioorganic Med. &amp; Chem. Ltrs.</i> 9:2237-2242 (1999). | <input type="checkbox"/> |                 |
|                                 | BQ                             | HAY et al., "Structure-Activity Relationships of 1,2,4-Benzotriazine 1,4-Dioxides as Hypoxia-Selective Analogues of Tirapazamine," <i>J. Med. Chem.</i> 46:169-182 (2003).   | <input type="checkbox"/> |                 |
|                                 | BR                             | HERNICK et al., "Design, Synthesis, and Biological Evaluation of Indolequinone Phosphoramidate Prodrugs Targeted to DT-diaphorase," <i>J. Med. Chem.</i> 45:3540-3548 (2002).  | <input type="checkbox"/> |                 |
|                                 | BS                             | HERNICK et al., "Studies on the Mechanisms of Activation of Indolequinone Phosphoramidate Prodrugs," <i>J. Med. Chem.</i> 46:148-154 (2003).   | <input type="checkbox"/> |                 |
| Examiner Signature              | /Rei Tsang Shiao/ (07/21/2008) |  |                          | Date Considered |

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## NON PATENT LITERATURE DOCUMENTS

| Examiner Initials * | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>2</sup>           |
|---------------------|-----------------------|---|--------------------------|
|                     | BT                    | KYLE et al., "Direct Assessment of Drug Penetration into Tissue Using a Novel Application of Three-Dimensional Cell Culture," <i>Cancer Research</i> , 64:6304-6309 (2004).   | <input type="checkbox"/> |
|                     | BU                    | LIN et al., "(o- and p- Nitrobenzylloxycarbonyl) -5-fluorouracil Derivatives as Potential Conjugated Bioreductive Alkylating Agents," <i>J. Med. Chem.</i> , 29:84-89 (1986).   | <input type="checkbox"/> |
|                     | BV                    | NAYLOR et al., "Recent Advances in Bioreductive Drug Targeting," <i>Mini Reviews in Med. Chem.</i> , 1:17-29 (2001).  | <input type="checkbox"/> |
|                     | BW                    | PAPOT et al., "Design of Selectively Activated Anticancer Prodrugs: Elimination and Cyclization Strategies," <i>Curr. Med. Chem. - Anti-Cancer Agents</i> , 2:155-185 (2002).   | <input type="checkbox"/> |
|                     | BX                    | PARVEEN et al., "2-Nitroimidazol-5-Ylmethyl as a Potential Bioreductively Activated Prodrug System: Reductively Triggered Release of the Parp Inhibitor 5-Bromoisoquinoline," <i>Bioorganic Med. &amp; Chem. Lett.</i> , 9:2031-2036 (1999).                    | <input type="checkbox"/> |
|                     | BY                    | ROFSTAD et al., "Hypoxia-induced metastasis of human melanoma cells: involvement of vascular endothelial growth factor-mediated angiogenesis," <i>Br. J. Cancer</i> , 80(11):1697-1707 (1999).  | <input type="checkbox"/> |
|                     | BZ                    | ROSEN et al., "Phase I Study of TLK286 (Telcya) Administered Weekly in Advanced Malignancies," <i>Clin. Cancer Res.</i> , 10:3689-3698 (2004).  | <input type="checkbox"/> |
|                     | CA                    | STEINBERG et al., "Synthesis and Evaluation of Pteric Acid-Conjugated Nitroheterocyclic Phosphoramidates as Folate Receptor - Targeted Alkylating Agents," <i>J. Med. Chem.</i> , 44:69-73 (2001).  | <input type="checkbox"/> |
|                     | CB                    | WAKSELMAN, M., "1,4- and 1,6- Eliminations from Hydroxy- and Amino-Substituted Benzyl Systems: Chemical and Biochemical Applications," <i>Nouv. J. Chim.</i> , 7(7):439-447 (1983).   | <input type="checkbox"/> |
|                     | CC                    | WEST et al., "A comparison of adriamycin and mAMS, II. Studies with V79 and human tumour multicellular spheroids," <i>Cancer Chemother. Pharmacol.</i> , 20:109-114 (1987).   | <input type="checkbox"/> |
|                     | CD                    | WORKMAN et al., "The experimental development of bioreductive drugs and their role in cancer therapy," <i>Cancer and Metastasis Rev.</i> , 12:73-82 (1993).   | <input type="checkbox"/> |

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